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> d his

     (FILE 'HOME' ENTERED AT 16:25:16 ON 10 JUN 2002)

     FILE 'CA, BIOSIS, MEDLINE' ENTERED AT 16:25:46 ON 10 JUN 2002
L1         88756 S FIBRINOGEN?
L2          3358 S ELASTASE INHIBITOR?
L3            18 S L1 (P) L2
L4            10 DUP REM L3 (8 DUPLICATES REMOVED)
L5           886 S EGLIN?
L6            11 S L5 AND L1
L7             8 DUP REM L6 (3 DUPLICATES REMOVED)
L8         80213 S PLASMINOGEN?
L9             2 S L8 AND L1 AND (L2 OR L5)
L10         4120 S L2 OR L5
L11            2 S L10 AND L1 AND L8
L12            0 S L10 (P) L1 (P) L8
L13           26 S L10 (P) L1
L14           15 DUP REM L13 (11 DUPLICATES REMOVED)
L15         8641 S L1 (P) L8
L16           26 S L10 (P) L1

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WEST

Help | Logout | Interrupt

Main Menu | Search Form | Posting Counts | Show S Numbers | Edit S Numbers | Preferences | Cases

Search Results -

Term	Documents
(4 SAME 1).USPT,PGPB,JPAB,EPAB,DWPI,TDBD.	1219
(L1 SAME L4).USPT,PGPB,JPAB,EPAB,DWPI,TDBD.	1219

Database: US Patents Full-Text Database; US Pre-Grant Publication Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Search: Refine Search

Recall Text | Clear

Search History

DATE: Monday, June 10, 2002 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=ADJ			
L9	l1 same l4	1219	L9
L8	l1 same l2	2	L8
L7	l1 same l3	9	L7
L6	l1 and l3 and l4	98	L6
L5	l1 same l3 same l4	2	L5
L4	plasminogen	9714	L4
L3	elastase inhibitor	1065	L3
L2	eglin	288	L2
L1	fibrinogen	9213	L1

END OF SEARCH HISTORY

L7: Entry 6 of 9 File: USPT Apr 6, 1999

DOCUMENT-IDENTIFIER: US 5891418 A
TITLE: Peptide-metal ion pharmaceutical constructs and applications

Brief Summary Paragraph Right (4):
Peptide Drugs. In recent years, a significant number of peptides have been discovered with various biological effects. These peptides are being explored for use as drugs, in treatment or prevention of a variety of diseases. There are significant limitations with use of peptide drugs, including extremely rapid clearance from the circulatory system, low affinity with some peptides, immunogenicity of larger peptide constructs, and lack of stability against proteolytic enzymes. However, there are peptides in use or under investigation as therapeutic agents for a number of conditions, including somatostatin analogues, arginine vasopression, oxytocin, luteinizing hormone releasing hormone, angiotensin converting enzyme, renin and elastase inhibitors, a variety of antagonists, including fibrinogen receptor antagonists, and the like. In addition, peptidomimetic antibiotics and peptide-based vaccines are also in use or development as human drugs.

WEST

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L7: Entry 4 of 9 File: USPT Sep 26, 2000

DOCUMENT-IDENTIFIER: US 6124107 A
TITLE: Assay for marker of human polymorphonuclear leukocyte elastase activity

Brief Summary Paragraph Right (1):
Human polymorphonuclear leukocyte elastase (PMNE) cleaves human fibrinogen at multiple sites. Cleavage of the A.alpha. chain at A.alpha.(Val.sup.360 -Ser.sup.361) generates a stable product as indicated by its presence in biological fluids. A radioimmunoassay (RIA) based on the A.alpha.(Val.sup.360) epitope of this cleavage site has been developed which allows the evaluation of the potency of elastase inhibitors to inhibit formation of cleavage products containing this neoepitope in a variety of in vitro cell biological situations. The RIA detects an endogenous A.alpha.(Val.sup.360) in normal human plasma and at elevated concentrations in cystic fibrosis plasma and in rheumatoid arthritis synovial fluid samples.

Brief Summary Paragraph Right (13):
Human fibrinogen is a hetero-dimeric glycoprotein consisting of 3 non-identical chains, A.alpha., B.beta. and .gamma.. PMNE cleaves human fibrinogen at multiple sites. Primary sites of cleavage include A.alpha.(Val.sup.21 -Glu.sup.22), A.alpha.(Val.sup.360 -Ser.sup.361), A.alpha.(Val.sup.450 -Ile.sup.451), A.alpha.(Val.sup.464 -Thr.sup.465), A.alpha.(Met.sup.476 -Asp.sup.477), A.alpha.(Thr.sup.568 -Ser.sup.569), .gamma.(Thr.sup.305 -Ser.sup.306), .gamma.(Val.sup.347 -Tyr.sup.348) and .gamma.(Ala.sup.357 -Ser.sup.358). We have developed two antipeptide antibodies, one of which specifically measures PMNE hydrolysis of fibrinogen at the A.alpha.(Val.sup.21 -Glu.sup.22) position to release a 21 residue N-terminal peptide, and a second which measures cleavage at A.alpha.(Val.sup.360 -Ser.sup.361), to release a 250 residue C-terminal fragment (FIG. 1). The A.alpha.(Val.sup.360) carboxyl terminal fragment remains associated with the .beta. and .gamma. chains of fibrinogen due to the disulfide network of the protein. Neither of the 2 specific antisera recognize intact fibrinogen. Both of these RIA allow the evaluation of the potency of PMNE inhibitors, such as elastase inhibitors, to inhibit fibrinopeptide neoepitope generation in whole blood stimulated with the calcium ionophore A23187. However, a major disadvantage of the A.alpha.(Val.sup.21) assay is the rapid in vivo clearance and metabolism of the peptide neoepitope A.alpha.(Val.sup.21) (t.sub.1/2 of 30 sec in both the dog and rhesus monkey). In an extensive series of experiments we were unable to detect the A.alpha.(Val.sup.21) neoepitope in normal human plasma or in plasma samples from PiZZ individuals, nor in plasma from from patients with cystic fibrosis, emphysema or chronic bronchitis.

Detailed Description Paragraph Right (3):
Human fibrinogen is a hetero-dimeric glycoprotein consisting of 3 non-identical chains, A.alpha., B.beta. and .gamma.. PMNE cleaves human fibrinogen at multiple sites. Primary sites of cleavage include A.alpha.(Val.sup.21 -Glu.sup.22), A.alpha.(Val.sup.360 -Ser.sup.361), A.alpha.(Val.sup.450 -Ile.sup.451), A.alpha.(Val.sup.464 -Thr.sup.465), A.alpha.(Met.sup.476 -Asp.sup.477), A.alpha.(Thr.sup.568 -Ser.sup.569), .gamma.(Thr.sup.305 -Ser.sup.306), .gamma.(Val.sup.347 -Tyr.sup.348) and .gamma.(Ala.sup.357 -Ser.sup.358). We have developed two antipeptide antibodies, one of which specifically measures PMNE hydrolysis of fibrinogen at the A.alpha.(Val.sup.21 -Glu.sup.22) position to release a 21 residue N-terminal peptide, and a second which measures cleavage at A.alpha.(Val.sup.360 -Ser.sup.361), to release a 250 residue C-terminal fragment (FIG. 1). The A.alpha.(Val.sup.360) carboxyl terminal fragment remains associated with the .beta. and .gamma. chains of fibrinogen due to the disulfide network of the protein. Neither of the 2 specific antisera recognize intact fibrinogen. Both of these RIAs

allow the evaluation of the potency of PMNE inhibitors, such as elastase inhibitors, to inhibit fibrinopeptide neoepitope generation in whole blood stimulated with the calcium ionophore A23187. However, a major disadvantage of the A.alpha.(Val.sup.21) assay is the rapid in vivo clearance and metabolism of the peptide neoepitope A.alpha.(Val.sup.21) (t.sub.1/2 of 30 sec in both the dog and rhesus monkey). In an extensive series of experiments we have been unable to detect the A.alpha.(Val.sup.21) neoepitope in normal human plasma or in plasma samples from PiZZ individuals, nor in plasma from from patients with cystic fibrosis, emphysema or chronic bronchitis.

Detailed Description Paragraph Right (37):
The above defined assay technology is used to monitor the activity of human elastase inhibitors of human leukocyte elastase activity in human and primate blood. Generally an elastase inhibitor is combined with whole blood or given to primates or humans and the effect of leukocyte elastase on fibrinogen is determined. Replicate aliquots of freshly-drawn heparinized whole human blood are prepared with concentrations of elastase inhibitor ranging up to about 300 .mu.g/ml. Following a brief pre-incubation with the incubator, a membrane perturbator, such as calcium ionophore A23187, is added at a concentration of between about 75 .mu.M and about 300 .mu.M. Non-membrane perturbator controls containing blood and perturbator-only controls are included to measure the extent of uninhibited peptide generation. All assay samples are incubated at about 37.degree. C. for about 25 minutes. The plasma is then prepared and assayed fibrinogen cleavage products as described above. Elastase inhibitors are capable of inhibiting the generation of fibrinogen cleavage products and the levels of inhibition are easily detected using this novel assay system.

Detailed Description Paragraph Right (38):
In vivo inhibition of fibrinogen cleavage products following treatment of primates with an elastase inhibitor is evaluated. Blood or fluid samples are collected both before and after treatment with either an elastase inhibitor or saline. Each heparinized blood sample is divided into about 4 aliquots (about 1 ml) and processed as described above. Treatment of an animal with an elastase inhibitor causes a marked reduction in the amount of elastase cleavage product produced.

Detailed Description Paragraph Right (39):
The ability of the novel assay to determine the presence of the unique fibrinogen cleavage products and to determine the relative amounts of these products is evaluated with blood from individuals genetically deficient in alpha 1-proteinase inhibitor (.alpha.1Pi), a normal serum elastase inhibitor. Individuals deficient in .alpha.1Pi, exhibit the PiZZ phenotype, and produce less than normal levels of circulating .alpha.1Pi which is a natural inhibitor of leukocyte elastase, Janoff, Am. Rev. Respir. Dis. 132: 417-433 (1985). Consequently individuals exhibiting the PIZZ phenotype would not have the capacity to inhibit elastase activity and they should have increased fibrinogen cleavage products when assayed by the above procedure. When heparinized blood is collected from individuals who possess the PiZZ phenotype and processed as described above and levels of specific cleavage peptide antigen are measured, they are higher than normal volunteers.

Detailed Description Paragraph Right (74):
The effect of the elastase inhibitor
3-Acetoxymethyl-1.alpha.-methoxy-6-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene
-2-(2-(S)carboxy-pyrrolidinecarboxamide)5,5-dioxide (Compound 1) on the calcium ionophore A23187-induced fibrinogen cleavage peptide production was evaluated. Replicate 2 ml aliquots of freshly-drawn heparinized whole human blood were prepared with concentrations of Compound 1 ranging up to 100 .mu.l/ml. Following a brief pre-incubation of 5 minutes at 37.degree. C., calcium ionophore A23187 was added to a final concentration of 150 .mu.M. Non-ionophore containing blood and ionophore-only (no inhibitor) controls were included to measure the extent of uninhibited peptide generation. All aliquots were incubated at 37.degree. C. for 25 minutes, the plasma collected, processed and assayed for fibrinogen cleavage peptide as described above. The results are shown in the following table.

Detailed Description Paragraph Right (78):
The blood samples drawn from the treated chimpanzee after infusion of the elastase inhibitor produced markedly lower levels of the fibrinogen peptide in response to calcium ionophore A23187. Fibrinogen cleavage peptide was not detected in the

non-ionophore treated blood samples from either animal. Over the course of 30 to 40 minutes, the amount of ionophore-stimulated peptide production in freshly-drawn samples gradually returned to the pretreatment level. No consistent change over time was observed in the untreated animal.

Detailed Description Paragraph Center (26):
Effect of An Elastase Inhibitor on Calcium Ionophore A23187-Stimulated Production of Fibrinogen Cleavage Peptide In The Blood of Normal Humans

Detailed Description Paragraph Center (27):
Effect of An Elastase Inhibitor on Calcium Ionophore A23187-Stimulated Production of Fibrinogen Cleavage Peptide In Primate Blood

WEST

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L7: Entry 3 of 9 File: USPT Dec 18, 2001

DOCUMENT-IDENTIFIER: US 6331285 B1
TITLE: Structurally determined cyclic metallo-constructs and applications

Brief Summary Paragraph Right (4):
Peptide Drugs. In recent years, a significant number of peptides with various biological effects have been discovered. These peptides are being explored for use as drugs, in treatment or prevention of a variety of diseases. There are significant limitations with use of peptide drugs, including extremely rapid clearance from the circulatory system, low target affinity with some peptides, immunogenicity of larger peptide constructs, and lack of stability against proteolytic enzymes. However, there are peptides in use or under investigation as therapeutic agents for a number of conditions, including somatostatin analogues, arginine vasopressin, oxytocin, luteinizing hormone releasing hormone, angiotensin-converting enzyme, renin and elastase inhibitors, as well as a variety of antagonists, including fibrinogen receptor antagonists, and the like. In addition, peptidomimetic antibiotics and peptide-based vaccines are also in use or development as human drugs.

WEST

Generate Collection Print

L8: Entry 1 of 2 File: USPT Jan 5, 1999

DOCUMENT-IDENTIFIER: US 5856090 A
TITLE: DNA-methylase linking reaction

Brief Summary Paragraph Right (20):
In one particularly preferred alternative, each of the polypeptide determinant genes within the plurality of plasmid-polypeptide determinant conjugates can be derived from a single parent polypeptide determinant gene by random mutagenesis. The parent polypeptide determinant gene can code for any polypeptide, including, but not limited to, glutathione S-transferase, estrogen receptor, triose phosphate isomerase, thrombin, plasminogen, tissue plasminogen activator, streptokinase, human insulin, erythropoietin, thrombopoietin, a fibrinogen type III domain or a protein including a fibrinogen type III domain, a DNA binding domain or a protein including a DNA binding domain, a helix-turn-helix DNA binding domain or a protein including a helix-turn-helix DNA binding domain, interleukin, HIV reverse transcriptase, HIV protease, renin, elastase, subtilisin, .alpha.-lytic protease, hirudin, omatin, kistin, or eglin C. In one preferred alternative, the parent polypeptide determinant gene is glutathione S-transferase.

Detailed Description Paragraph Right (43):
The polypeptide determinant can be any single polypeptide chain expressible in a prokaryotic system, generally E. coli. There are no fixed length restrictions on the polypeptide determinant; it can be a short peptide or a long protein chain. It can be an intact protein or single subunit of a multi-subunit protein. Alternatively, it can be a structural or functional domain of a protein, or a fragment of a protein or peptide produced by proteolytic cleavage, either chemical or enzymatic. The polypeptide determinant can also be a synthetic or naturally occurring peptide. Typical polypeptide determinants include, but are not necessarily limited to, glutathione S-transferase, estrogen receptor, triose phosphate isomerase, thrombin, plasminogen, tissue plasminogen activator, streptokinase, human insulin, erythropoietin, thrombopoietin, a fibrinogen type III domain or a protein including a fibrinogen type III domain, a DNA binding domain or a protein including a binding domain, a helix-turn-helix DNA binding domain or a protein including a helix-turn-helix DNA binding domain, interleukin, interferon, HIV reverse transcriptase, HIV protease, renin, elastase, subtilisin, .alpha.-lytic protease, hirudin, omatin, kistin, and eglin C.

CLAIMS:

35. The library of claim 34 wherein the parent polypeptide determinant gene encodes a protein selected from the group consisting of glutathione S-transferase, estrogen receptor, triose phosphate isomerase, thrombin, plasminogen, tissue plasminogen activator, streptokinase, human insulin, erythropoietin, thrombopoietin, a fibrinogen type III domain or a protein including a fibrinogen type III domain, a DNA binding domain or a protein including a DNA binding domain, a helix-turn-helix DNA binding domain or a protein including a helix-turn-helix DNA binding domain, interleukin, HIV reverse transcriptase, HIV protease, renin, elastase, subtilisin, .alpha.-lytic protease, hirudin, omatin, kistin, and eglin C.

43. The method of claim 36 wherein the polypeptide determinant gene encodes a protein selected from the group consisting of glutathione S-transferase, estrogen receptor, triose phosphate isomerase, thrombin, plasminogen, tissue plasminogen activator, streptokinase, human insulin, erythropoietin, thrombopoietin, a fibrinogen type III domain or a protein including a fibrinogen type III domain, a DNA binding domain or a

protein including a DNA binding domain, a helix-turn-helix DNA binding domain or a protein including a helix-turn-helix DNA binding domain, interleukin, HIV reverse transcriptase, HIV protease, renin, elastase, subtilisin, .alpha.-lytic protease, hirudin, omatin, kistin, and eglin C.

WEST

End of Result Set

Generate Collection | Print

L7: Entry 9 of 9 File: DWPI May 17, 1996

DERWENT-ACC-NO: 1996-251888
DERWENT-WEEK: 200057

TITLE: New isolated fibrinogen derived cleavage products - used for detection of leukocyte elastase activity in disease diagnosis and for evaluating elastase inhibitors

INVENTOR: BOGER, J S; DAHLGREN, M E ; DAVIES, D T P ; HUMES, J L ; MUMFORD, R A

PATENT-ASSIGNEE:

ASSIGNEE	CODE
MERCK & CO INC	MERI

PRIORITY-DATA: 1995US-0469141 (June 6, 1995), 1994US-0335524 (November 7, 1994), 1988US-0205416 (June 10, 1988), 1991US-0674280 (March 21, 1991), 1992US-0902102 (June 22, 1992), 1994US-0196663 (February 15, 1994)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 9614580 A1	May 17, 1996	E	109	G01N033/53
US 6124107 A	September 26, 2000		000	G01N033/53

DESIGNATED-STATES: CA JP US AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE

CITED-DOCUMENTS:05Jnl.Ref; EP 345906 ; US 5157019

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
WO 9614580A1	November 3, 1995	1995WO-US13794	
US 6124107A	June 10, 1988	1988US-0205416	Cont of
US 6124107A	March 21, 1991	1991US-0674280	Cont of
US 6124107A	June 22, 1992	1992US-0902102	Cont of
US 6124107A	February 15, 1994	1994US-0196663	CIP of
US 6124107A	November 7, 1994	1994US-0335524	CIP of
US 6124107A	June 6, 1995	1995US-0469141	

INT-CL (IPC): C07 K 7/00; G01 N 33/53; G01 N 33/555; G01 N 33/567

ABSTRACTED-PUB-NO: US 6124107A
BASIC-ABSTRACT:

A novel isolated and purified peptide comprises an epitope which includes the terminal amino acid sequence of the C-terminus of the primary cleavage prods. of human leukocyte elastase (HLE) cleaved human fibrinogen (Fg), which is capable of inducing specific antibodies and acting as a specific probe for the detection of the antibodies.

USE - The prods. and methods can be used for the detection of leukocyte

elastase cleavage prods. and for the evaluation of leukocyte elastase inhibitors. They can be used to diagnose and monitor diseases such as arthritis, gout, pulmonary emphysema, chronic bronchitis, cystic fibrosis, chronic obstructive pulmonary disease, bronchiectasis, adult or infantile respiratory distress syndrome and myelogenous leukaemia.

ADVANTAGE - The assay method allows for the rapid and reproducible detection of HLE-specific cleavage peptides.
ABSTRACTED-PUB-NO:

WO 9614580A
EQUIVALENT-ABSTRACTS:

A novel isolated and purified peptide comprises an epitope which includes the terminal amino acid sequence of the C-terminus of the primary cleavage prods. of human leukocyte elastase (HLE) cleaved human fibrinogen (Fg), which is capable of inducing specific antibodies and acting as a specific probe for the detection of the antibodies.

USE - The prods. and methods can be used for the detection of leukocyte elastase cleavage prods. and for the evaluation of leukocyte elastase inhibitors. They can be used to diagnose and monitor diseases such as arthritis, gout, pulmonary emphysema, chronic bronchitis, cystic fibrosis, chronic obstructive pulmonary disease, bronchiectasis, adult or infantile respiratory distress syndrome and myelogenous leukaemia.

ADVANTAGE - The assay method allows for the rapid and reproducible detection of HLE-specific cleavage peptides.

CHOSEN-DRAWING: Dwg.0/24

TITLE-TERMS: NEW ISOLATE FIBRINOGEN DERIVATIVE CLEAVE PRODUCT DETECT LEUCOCYTE ELASTASE ACTIVE DISEASE DIAGNOSE EVALUATE ELASTASE INHIBIT

DERWENT-CLASS: B04 D16 S03

CPI-CODES: B04-G01; B04-H19; B04-L05C; B04-M01; B11-C07A; B12-K04A; D05-H09; D05-H11; D05-H17A5;

EPI-CODES: S03-E14H4;

CHEMICAL-CODES:

Chemical Indexing M1 *01*
Fragmentation Code
M423 M710 M781 M903 N102 P831 Q233 V752

Chemical Indexing M1 *02*
Fragmentation Code
M423 M710 M903 Q233 V600 V611

Chemical Indexing M1 *03*
Fragmentation Code
M423 M750 M903 N102 Q233 V802 V815

Chemical Indexing M6 *04*
Fragmentation Code
M903 P831 Q233 R515 R521 R627 R632

SECONDARY-ACC-NO:
CPI Secondary Accession Numbers: C1996-079795
Non-CPI Secondary Accession Numbers: N1996-211618

WEST

Generate Collection Print 09/486,516

L7: Entry 5 of 9 File: USPT Feb 22, 2000

DOCUMENT-IDENTIFIER: US 6027711 A
TITLE: Structurally determined metallo-constructs and applications

Brief Summary Paragraph Right (4):
Peptide Drugs. In recent years, a significant number of peptides with various biological effects have been discovered. These peptides are being explored for use as drugs, in treatment or prevention of a variety of diseases. There are significant limitations with use of peptide drugs, including extremely rapid clearance from the circulatory system, low target affinity with some peptides, immunogenicity of larger peptide constructs, and lack of stability against proteolytic enzymes. However, there are peptides in use or under investigation as therapeutic agents for a number of conditions, including somatostatin analogues, arginine vasopressin, oxytocin, luteinizing hormone releasing hormone, angiotensin-converting enzyme, renin and elastase inhibitors, as well as a variety of antagonists, including fibrinogen receptor antagonists, and the like. In addition, peptidomimetic antibiotics and peptide-based vaccines are also in use or development as human drugs.

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Jan 25	BLAST(R) searching in REGISTRY available in STN on the Web
NEWS 3	Jan 29	FSTA has been reloaded and moves to weekly updates
NEWS 4	Feb 01	DKILIT now produced by FIZ Karlsruhe and has a new update frequency
NEWS 5	Feb 19	Access via Tymnet and SprintNet Eliminated Effective 3/31/02
NEWS 6	Mar 08	Gene Names now available in BIOSIS
NEWS 7	Mar 22	TOXLIT no longer available
NEWS 8	Mar 22	TRCTHERMO no longer available
NEWS 9	Mar 28	US Provisional Priorities searched with P in CA/CAplus and USPATFULL
NEWS 10	Mar 28	LIPINSKI/CALC added for property searching in REGISTRY
NEWS 11	Apr 02	PAPERCHEM no longer available on STN. Use PAPERCHEM2 instead.
NEWS 12	Apr 08	"Ask CAS" for self-help around the clock
NEWS 13	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 14	Apr 09	ZDB will be removed from STN
NEWS 15	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 16	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 17	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 18	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 19	Jun 03	New e-mail delivery for search results now available
NEWS 20	Jun 10	MEDLINE Reload
NEWS 21	Jun 10	PCTFULL has been reloaded

NEWS EXPRESS	February 1 CURRENT WINDOWS VERSION IS V6.0d, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 16:25:16 ON 10 JUN 2002

=> file ca, biosis, medline
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'CA' ENTERED AT 16:25:46 ON 10 JUN 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE 'BIOSIS' ENTERED AT 16:25:46 ON 10 JUN 2002
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'MEDLINE' ENTERED AT 16:25:46 ON 10 JUN 2002

=> s fibrinogen?
L1        88756 FIBRINOGEN?

=> s elastase inhibitor?
L2         3358 ELASTASE INHIBITOR?

=> s l1 (p) l2
L3           18 L1 (P) L2

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4           10 DUP REM L3 (8 DUPLICATES REMOVED)

=> d 1-10 ab,bib

L4   ANSWER 1 OF 10  CA  COPYRIGHT 2002 ACS
AB   The invention provides a method for reducing or preventing adhesions
which
     would form in a patient during or after surgery, said method comprising
     administering to said patient an effective amt. of a fibrinogen prepn.
     contg. a non-plasmin acting fibrinolysis inhibitor.  The invention also
     provides the use of a non-plasmin acting fibrinolysis inhibitor in the
     prepn. of a fibrinogen prepn. for the redn. or prevention of postsurgical
     adhesions.
AN   136:289068  CA
TI   Fibrinogen plus a non-plasmin-acting fibrinolysis inhibitor for the
     reduction or prevention of adhesion formation following surgery
IN   Redl, Heinz
PA   Baxter International Inc., USA; Baxter Healthcare S.A.
SO   PCT Int. Appl., 16 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
PI   WO 2002030445      A2   20020418       WO 2001-US32043  20011012
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
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PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI US 2000-240438P P 20001013

L4 ANSWER 2 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:131559 BIOSIS
DN PREV200100131559
TI The effect of virus inactivation on coagulation factors in therapeutic plasma.
AU Zeiler, T. (1); Wittmann, G.; Zimmermann, R.; Hintz, G.; Huhn, D.; Riess, H.
CS (1) Department of Transfusion Medicine and Haemostaseology, University Clinics, Philipps-University Marburg, Berlin:
zeiler@mailer.uni-marburg.de
Germany
SO British Journal of Haematology, (December, 2000) Vol. 111, No. 3, pp. 986-987. print.
ISSN: 0007-1048.
DT Letter
LA English
SL English

L4 ANSWER 3 OF 10 CA COPYRIGHT 2002 ACS
AB A **fibrinogen**-based tissue adhesive (fibrin glue) contains an **elastase inhibitor** to stabilize the adhesive in vivo against premature fibrinolysis. The **elastase inhibitor** (e.g. eglin, elastase-.alpha.1-proteinase inhibitor, .alpha.1-antiprotease, elafin, leukocyte proteinase inhibitor) is effective even in
the absence of plasmin inhibitors such as aprotinin, and is preferably a human or recombinant human protein. It is used in a proportion of .gtoreq.10-6 U/g **fibrinogen**, preferably 10-3-10 U/g.
AN 130:213685 CA
TI Fibrinogen-based tissue adhesive
IN Redl, Heinz; Schlag, Guenther; Eibl, Johann
PA Immuno Aktiengesellschaft, Austria
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9911301	A1	19990311	WO 1998-AT202	19980826
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AT 9701449	A	19990715	AT 1997-1449	19970828
AT 406120	B	20000225		
AU 9889637	A1	19990322	AU 1998-89637	19980826
EP 1007109	A1	20000614	EP 1998-941134	19980826
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, FI
JP 2001514050 T2 20010911 JP 2000-508402 19980826
PRAI AT 1997-1449 A 19970828
WO 1998-AT202 W 19980826
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 10 CA COPYRIGHT 2002 ACS DUPLICATE 1
AB Upon stimulation, polymorphonuclear leukocytes (PMNs) release potent serine proteases, i.e. elastase, cathepsin G and proteinase 3, which contribute to the degrdn. of tissue and plasma components. Here, we describe the development of a plasma test to assess PMN-mediated **fibrinogenolysis** as a biochem. marker for actual PMN-derived proteolysis in vivo, useful for monitoring therapeutic efficacy, i.e. of **elastase inhibitors**. We generated a monoclonal antibody (MAb), designated 1-1/B3, with a high affinity for elastase-degraded **fibrinogen** (EDF). The epitope for 1-1/B3 becomes exposed in a time-dependent manner during digestion of **fibrinogen** with purified PMN-derived serine proteases and with isolated PMNs in vitro. However, 1-1/B3 does not react with plasma **fibrinogen** or with fibrin(ogen) degrdn. products generated by plasmin or by other active proteases that may occur locally, i.e. metalloproteases and lysosomal cathepsins. On the basis of MAb 1-1/B3, we developed a plasma test for the assessment of PMN-mediated fibrin(ogen) degrdn. products (PMN-FDP). In a panel of control plasmas, we obsd. concns. of PMN-FDP of 8.cntdot.2 .+-. 0.cntdot.9 ng mL-1 (n = 18). These values were increased twofold in patients with .alpha.1-proteinase inhibitor deficiency (18.cntdot.6 .+-. 3.cntdot.3 ng mL-1; n = 12; P < 0.cntdot.0001) and even more in patients with sepsis (365.cntdot.7 .+-. 97.cntdot.7 ng mL-1; n = 16; P < 0.cntdot.0001). Furthermore, synovial tissue exts. from patients with rheumatoid arthritis contained increased levels of PMN-FDP, compared with synovial tissue exts. (P < 0.cntdot.005) from patients with osteoarthritis.
AN 126:235523 CA
TI An enzyme immunoassay for polymorphonuclear leukocyte-mediated fibrinogenolysis
AU Bos, R.; Van Leuven, C. J. M.; Stolk, J.; Hiemstra, P. S.; Ronday, H. K.; Nieuwenhuizen, W.
CS TNO-Prevention and Health, Division of Vascular and Connective Tissue Research, Leiden, 2301 CE, Neth.
SO Eur. J. Clin. Invest. (1997), 27(2), 148-156
CODEN: EJCIB8; ISSN: 0014-2972
PB Blackwell
DT Journal
LA English

L4 ANSWER 5 OF 10 CA COPYRIGHT 2002 ACS DUPLICATE 2
AB The relation of biol. markers of extracellular matrix (plasma elastin peptides and **elastase inhibitors**) to the clin. history of cardiovascular diseases and risk factors for atherosclerosis were examd. in a large population study (the EVA Study) on vascular and cognitive aging performed in 1389 men and women 59-71 yr. A moderate decrease in elastin peptides was obsd. in women with a self-reported history of coronary heart disease and stroke as well as with diabetes. Similar but non-significant trends were found in men. Furthermore, elastin peptides were significantly and pos. correlated to HDL-cholesterol and apolipoprotein A1 in both sexes. **Elastase inhibitor** titers were significantly higher in women than in men. A moderate increase was found in men and women with a history of coronary heart

disease that reached significance level after pooling both sexes. Furthermore, **elastase inhibitor** titers were significantly and pos. related to **fibrinogen** and C reactive protein in either sex. No consistent assocns. were obsd. between both biol. markers of extracellular matrix and age, blood pressure, body mass index and tobacco or alc. consumption. These results suggested that a decrease in elastin peptides and an increase in **elastase inhibitors** might be assocd. with risk factors of atherogenesis as well as with atherosclerosis-related diseases.

AN 127:93576 CA
TI Aging of the vascular wall: serum concentration of elastin peptides and elastase inhibitors in relation to cardiovascular risk factors. The EVA study
AU Bizbiz, L.; Alperovitch, A.; Robert, L.
CS EVA Group, Lab. Biol. Cellulaire, Univ. Paris VII, Paris, 75005, Fr.
SO Atherosclerosis (Shannon, Ireland) (1997), 131(1), 73-78
CODEN: ATHSBL; ISSN: 0021-9150
PB Elsevier
DT Journal
LA English

L4 ANSWER 6 OF 10 MEDLINE
AB The patterns of degradation and the influence of factor XIII polymerization on fibrin stability were examined in vitro following incubation with leukocyte elastase. In vivo experiments, various factor XIII-polymerized fibrin clots were implanted subcutaneously in mice to evaluate the stability of clots in the extravascular space. Both in vitro and in vivo lysis proceeded faster with nonpolymerized fibrin and was not influenced by the presence of cross-linked alpha 2-plasmin inhibitor. In vivo lysis of implanted clots was prevented by elastatinal, powerful **elastase inhibitor**, suggesting that granulocyte elastase is chiefly responsible for clot lysis in the extravascular space. To further extend investigations on the mechanisms of fibrinolysis in tissues, we evaluated fibrin and its degradation products in the synovial space. Expression of factor XIII in synovial cells and activities of coagulation factors, fibrinolytic enzymes, and inhibitors were investigated in the synovial fluid of rheumatoid arthritis patients. Immunohistochemical analysis showed deposits of insoluble fibrin on synovial membranes and pannus to an extent related to the progression of the disease. Factor XIII was expressed by fibroblasts and macrophages in the early stages of the disease, whereas in advanced stages factor XIII staining was associated with fibrin. The reduction of certain coagulation factors and high level of thrombin-antithrombin complexes in synovial fluid show a steady activation of the coagulation cascade. The evaluation of **fibrinogen** degradation products and the pattern of degradation of synovial fibrin(ogen) suggest the participation of leukocyte elastase in fibrin(ogen) lysis in synovial tissue of rheumatoid arthritis.

AN 97192399 MEDLINE
DN 97192399 PubMed ID: 9122713
TI Fibrin degradation in the synovial fluid of rheumatoid arthritis patients:
a model for extravascular fibrinolysis.
AU Carmassi F; de Negri F; Morale M; Song K Y; Chung S I
CS 2nd Medical Clinic, University of Pisa, Italy.
SO SEMINARS IN THROMBOSIS AND HEMOSTASIS, (1996) 22 (6) 489-96. Ref: 90
Journal code: 0431155. ISSN: 0094-6176.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199704
ED Entered STN: 19970506
Last Updated on STN: 19970506
Entered Medline: 19970424

L4 ANSWER 7 OF 10 CA COPYRIGHT 2002 ACS
AB Incubation of human blood with the secretagogue A23187 resulted in the formation of increased plasma concns. of polymorphonuclear leukocyte (PMN) elastase:.alpha.1 proteinase inhibitor (PMNE:.alpha.1PI) complex as well as A.alpha.(1-21) fibrinopeptide [A.alpha.(1-21)]. The formation of these species was both time and A23187 concn. dependent. Using a sandwich ELISA and a RIA, we detd. the comparative potencies of several compds. to inhibit the formation of PMNE:.alpha.1PI complexes and A.alpha.(1-21), resp. L-658,758, a substituted cephalosporin, essentially irreversible elastase inhibitor, inhibited the formation of PMNE:.alpha.1PI and A.alpha.(1-21) with IC50 values of 38 and 15 .mu.M, resp. L-683,845, a monocyclic .beta.-lactam, was much more potent against isolated PMNE than L-658,758. However in this system it was approx. equiv. to L-658,758 with an IC50 of 15 .mu.M against both species. ICI-200,880, a competitive slow-binding elastase inhibitor, was significantly less potent to inhibit A.alpha.(1-21), having an IC50 of 75 .mu.M, while Declaben, a reversible noncompetitive inhibitor, was inactive at concns. as great as 200 .mu.M. We propose that evaluating inhibitors in the complex milieu of blood will provide a useful method to predict their therapeutic potential in vivo.
AN 123:187603 CA
TI Formation of polymorphonuclear leukocyte elastase:.alpha.1 proteinase inhibitor complex and A.alpha.(1-21) fibrinopeptide in human blood stimulated with the calcium ionophore A23187. A model to characterize inhibitors of polymorphonuclear leukocyte elastase
AU Pacholok, Stephen G.; Davies, Philip; Dorn, Conrad; Finke, Paul; Hanlon, William A.; Mumford, Richard A.; Humes, John L.
CS Merck Res. Labs., Rahway, NJ, 07065, USA
SO Biochem. Pharmacol. (1995), 49(10), 1513-20
CODEN: BCPCA6; ISSN: 0006-2952
DT Journal
LA English

L4 ANSWER 8 OF 10 CA COPYRIGHT 2002 ACS DUPLICATE 3
AB Acute respiratory failure is a common complication in patients with disseminated intravascular coagulation assocd. with sepsis. To elucidate the role of coagulation abnormalities in acute lung injury in sepsis, the authors investigated the effect of anticoagulants on the pulmonary vascular injury in rat induced by lipopolysaccharide (LPS). When administered i.v., LPS (5 mg/kg body wt.) increased the accumulation of 111indium-labeled neutrophils in lung 30 min after administration. Subsequently, the pulmonary vascular permeability and the serum level of fibrin and **fibrinogen** degrdn. products (E) [FDP (E)] increased and remained elevated for several hours. Neither heparin alone, heparin plus antithrombin III, or dansyl-Glu-Gly-Arg-chloromethyl ketone-treated factor Xa, a selective inhibitor of thrombin generation, prevented LPS-induced vascular injury 6 h after LPS administration, whereas these substances inhibited the increase in serum FDP (E) at that time. LPS-induced pulmonary vascular injury was attenuated in rats with

methotrexate-induced leukocytopenia or treated with ONO-5046, a potent granulocyte **elastase inhibitor**, although ONO-5046 did not inhibit the LPS-induced increase in serum FDP (E). Thus, activated leukocytes play a more important role than coagulation abnormalities in the pathogenesis of LPS-induced pulmonary vascular injury in an exptl. rat model of endotoxemia.

AN 122:262617 CA
TI Endotoxin-induced pulmonary vascular injury is mainly mediated by activated neutrophils in rats
AU Uchiba, Mitsuhiro; Okajima, Kenji; Murakami, Kazunori; Okabe, Hiroaki; Takatsuki, Kiyoshi
CS Department of Medicine, Kumamoto University Medical School, Kumamoto, Japan
SO Thromb. Res. (1995), 78(2), 117-25
CODEN: THBRAA; ISSN: 0049-3848
DT Journal
LA English

L4 ANSWER 9 OF 10 CA COPYRIGHT 2002 ACS DUPLICATE 4
AB Tryptase from human mast cells has been shown (in vitro) to catalyze the destruction of **fibrinogen** and high-mol.-wt. kininogen as well as the activation of complement C3a and collagenase. Although large amts. of tryptase are released in tissues by degranulating mast cells and levels .ltoreq.1000 ng/mL have been measured in the circulation following systemic anaphylaxis, no specific physiol. inhibitor has yet been found for the protease. The current work tests several more inhibitors for their effects on tryptase and examines any effect of tryptase on these inhibitors. First, antileukoprotease and low-mol.-wt. **elastase inhibitor** from human lung and hirudin and antithrombin III had no effect on tryptase activity in vitro. Second, the possibility that tryptase, being insensitive to the effects of inhibitors, might instead destroy them was also considered. Tryptase failed to cleave and inactivate antileukoprotease, low-mol.-wt. **elastase inhibitor**, .alpha.1-protease inhibitor, .alpha.2-macroglobulin, and antithrombin III. Third, based on the knowledge that tryptase stability is regulated by its interaction with heparin, antithrombin III was used as a model heparin-binding protein to demonstrate that a protein competitor for heparin-binding sites, presumably by displacement of tryptase, destabilizes this enzyme. Conversely, tryptase, in excess, blocked the binding of antithrombin III to heparin, thereby attenuating the heparin-mediated inhibition of thrombin by antithrombin III.

AN 112:114729 CA
TI Interactions of human mast cell tryptase with biological protease inhibitors
AU Alter, Stephen C.; Kramps, Johannes A.; Janoff, Aaron; Schwartz, Lawrence B.
CS Dep. Med., Med. Coll. Virginia, Richmond, VA, 23298, USA
SO Arch. Biochem. Biophys. (1990), 276(1), 26-31
CODEN: ABBIA4; ISSN: 0003-9861
DT Journal
LA English

L4 ANSWER 10 OF 10 CA COPYRIGHT 2002 ACS
AB Inhibitors for chymotrypsin, trypsin, elastase, and plasmin were studied in 18 horses with **fibrinogen** plate electrophoresis. Plasmin was mainly inhibited by .alpha.2-macroglobulin (.alpha.2M). Besides .alpha.2M, an anodically migrating group of inhibitors in the albumin-prealbumin region was responsible for inhibition of chymotrypsin,

trypsin, and elastase. These inhibitors were heterogeneous. Three inhibitors for chymotrypsin, 3 for trypsin, and .gtoreq.2 for elastase were identified. Not more than 2 inhibitors for 1 enzyme were present in the serum of a single animal. The banding patterns showed individual differences. Four patterns for chymotrypsin and 3 for trypsin could be distinguished in the 18 horses studied. **Elastase inhibitors** showed fewer individual differences. This may partly be due to the low resolving power of the method used. The possible implications of the heterogeneity of the inhibitors for the pathogenesis of chronic obstructive lung diseases are discussed.

AN 90:135633 CA
TI Electrophoretic analysis of protease inhibitors in horses serum
AU Von Fellenberg, R.
CS Inst. Veterinaerphysiol., Univ. Zurich, Zurich, Switz.
SO Schweiz. Arch. Tierheilkd. (1978), 120(12), 631-42
CODEN: SATHAA; ISSN: 0036-7281
DT Journal
LA German

=> s eglin?
L5 886 EGLIN?

=> d his

(FILE 'HOME' ENTERED AT 16:25:16 ON 10 JUN 2002)

FILE 'CA, BIOSIS, MEDLINE' ENTERED AT 16:25:46 ON 10 JUN 2002
L1 88756 S FIBRINOGEN?
L2 3358 S ELASTASE INHIBITOR?
L3 18 S L1 (P) L2
L4 10 DUP REM L3 (8 DUPLICATES REMOVED)
L5 886 S EGLIN?

=> s l5 and l1
L6 11 L5 AND L1

=> dup rem l6
PROCESSING COMPLETED FOR L6
L7 8 DUP REM L6 (3 DUPLICATES REMOVED)

=> d ab,bib 1-8

L7 ANSWER 1 OF 8 CA COPYRIGHT 2002 ACS
AB The invention provides a method for reducing or preventing adhesions which would form in a patient during or after surgery, said method comprising administering to said patient an effective amt. of a **fibrinogen** prepn. contg. a non-plasmin acting fibrinolysis inhibitor. The invention also provides the use of a non-plasmin acting fibrinolysis inhibitor in the prepn. of a **fibrinogen** prepn. for the redn. or prevention of postsurgical adhesions.
AN 136:289068 CA
TI **Fibrinogen** plus a non-plasmin-acting fibrinolysis inhibitor for the reduction or prevention of adhesion formation following surgery
IN Redl, Heinz
PA Baxter International Inc., USA; Baxter Healthcare S.A.
SO PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DT Patent

LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002030445	A2	20020418	WO 2001-US32043	20011012

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-240438P P 20001013

L7 ANSWER 2 OF 8 CA COPYRIGHT 2002 ACS

AB A **fibrinogen**-based tissue adhesive (fibrin glue) contains an elastase inhibitor to stabilize the adhesive in vivo against premature fibrinolysis. The elastase inhibitor (e.g. **eglin**, elastase-.alpha.1-proteinase inhibitor, .alpha.1-antiprotease, elafin, leukocyte proteinase inhibitor) is effective even in the absence of plasmin inhibitors such as aprotinin, and is preferably a human or recombinant human protein. It is used in a proportion of .gtoreq.10-6 U/g

fibrinogen, preferably 10-3-10 U/g.

AN 130:213685 CA

TI **Fibrinogen**-based tissue adhesive

IN Redl, Heinz; Schlag, Guenther; Eibl, Johann

PA Immuno Aktiengesellschaft, Austria

SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9911301	A1	19990311	WO 1998-AT202	19980826

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	AT 9701449	A	19990715	AT 1997-1449	19970828
	AT 406120	B	20000225		
	AU 9889637	A1	19990322	AU 1998-89637	19980826
	EP 1007109	A1	20000614	EP 1998-941134	19980826

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI

	JP 2001514050	T2	20010911	JP 2000-508402	19980826
PRAI	AT 1997-1449	A	19970828		
	WO 1998-AT202	W	19980826		

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 8 CA COPYRIGHT 2002 ACS DUPLICATE 1

AB Leukocyte initiation of coagulation preserves the hematostatic balance and

may aberrantly contribute to vascular injury. In addn. to the extrinsic activation mediated by tissue factor: factor VIIa, monocytes express an alternative procoagulant response after binding of the zymogen factor X to the integrin Mac-1 (CD11b/CD18). Here, factor X-activating activity was found in purified monocyte granules, and coincided with size-chromatographed fractions contg. cathepsin G. In contrast, elastase-contg. granule fractions did not activate factor X. In the presence of Ca2+ ions, purified cathepsin G, but not elastase, cleaved factor X to a .apprx.54 kDa catalytically active deriv., structurally indistinguishable from the procoagulant product generated on monocytes after binding to Mac-1. Factor X activation by purified cathepsin G involved limited proteolysis of a novel Leu177-Leu178 peptide bond in the zymogen's activation peptide. Cathepsin G activation of factor X was completely inhibited by .alpha.1 antitrypsin, .alpha.1 antichymotrypsin, or soybean trypsin inhibitor, or by a neutralizing antiserum to cathepsin G, while **eglin**, or an anti-elastase antibody, were ineffective. Affinity chromatog. on active-site-dependent inhibitors Glu-Gly-Arg-chloromethyl ketone or benzamidine completely abolished factor Xa activity generated by cathepsin G. Cathepsin G was not constitutively detected on the monocyte surface by flow cytometry. However, inflammatory stimuli, including formyl peptide or phorbol ester, or Mac-1 engagement with its ligands **fibrinogen**, factor X or serum-opsonized zymosan, triggered monocyte degranulation and cathepsin G activation of factor X. These findings demonstrate that monocytes can alternatively initiate coagulation in a sequential three-step cascade, including (i) binding of factor X to Mac-1, (ii) discharge of azurophil granules, and (iii) limited proteolytic activation of membrane-bound factor X by cathepsin G. By rapidly forming thrombin and factor Xa in a protected membrane microenvironment, this pathway may contribute a priming signal for clotting, anticoagulation and visual cell signal transduction, in vivo.

AN 126:17537 CA
TI Activation of Mac-1 (CD11b/CD18)-bound factor X by released cathepsin G defines an alternative pathway of leukocyte initiation of coagulation
AU Plescia, Janet; Altieri, Dario C.
CS Boyer Center Molecular Medicine, Yale University School Medicine, New Haven, CT, 06536, USA
SO Biochem. J. (1996), 319(3), 873-879
CODEN: BIJOAK; ISSN: 0264-6021
PB Portland Press
DT Journal
LA English

L7 ANSWER 4 OF 8 CA COPYRIGHT 2002 ACS
AB Human polymorphonuclear leukocytes (PMN) activated by fMLP (in the presence of CaCl2, **fibrinogen**, and cytochalasin B) were able to induce aggregation, cytoplasmic Ca2+ increase, and thromboxane A2 prodn. in coincubated autologous platelets. Cell-free supernatants prepd. from formyl-methionyl-leucyl-phenylalanine (fMLP)-stimulated PMN were able also to induce platelet activation. Antibodies against cathepsin G and different serine protease inhibitors completely suppressed the activity of PMN-derived supernatants, indicating that cathepsin G is the major platelet activator released by PMN in the system. However, antiproteinases only partially affected platelet activation induced by PMN

in mixed cell suspensions. Superoxide dismutase and catalase added to the cell suspension did not affect platelet activation nor potentiate serine protease inhibitors, making a role for short-lived O radicals in this exptl. system unlikely. Electron microscopic observation of stirred mixed cell suspensions preincubated for 2 min at 37.degree. before stimulation showed a close PMN-platelets contact without any morphol. or biochem. event suggesting platelet activation. Preincubation of the cells without stirring to minimize PMN-platelet interaction before stimulation did not modify subsequent aggregation and platelet cytoplasmic Ca2+ increase in control samples. However, trypsin inhibitor from soybean completely prevented PMN-induced platelet activation. In samples preincubated without stirring in the presence of the antiproteinase, activated PMN adhered together but platelets preserved their discoid shape and did not appear significantly activated. It is proposed that membrane-to-membrane contact could create a microenvironment in which cathepsin G, discharged from stimulated PMN on adherent platelets, is protected from antiproteinases.

AN 115:26692 CA

TI Platelet activation by fMLP-stimulated polymorphonuclear leukocytes: the activity of cathepsin G is not prevented by antiproteinases

AU Evangelista, Virgilio; Rajtar, Grazyna; De Gaetano, Giovanni; White, James G.; Cerletti, Chiara

CS Giulio Bizzozero Lab. Platelet Leukocyte Pharmacol., Ist. Ric. Farmacol. Mario Negri, Santa Maria Imbaro, 66030, Italy

SO Blood (1991), 77(11), 2379-88
CODEN: BLOOAW; ISSN: 0006-4971

DT Journal

LA English

L7 ANSWER 5 OF 8 CA COPYRIGHT 2002 ACS

AB A simple purifn. method which is able to sep. leukocyte cathepsin G (I) from leukocyte elastase (II) is described. I was purified on an affinity column contg. Suc-Tyr-D-Leu-D-Val-pNA-Sepharose (Suc = succinyl; pNA = p-nitroanilide). I in leukocyte exts. adsorbed to the column at low concns. of NaCl (0.2M), and was eluted with Tris-HCl buffer (0.1M, pH 7.5) contg. 2M NaCl. The purified I prepn. contained no II activity. Although the proteolytic activity of I against **fibrinogen** and fibrin was very weak compared with that of II, I acted synergistically with II in the **fibrinogenolysis**. Furthermore, the effect was dependent on the amt. of I. The inhibitory effects of **eglin** c fragments for I and II were different. The Ki values of the H-(41-49)-OMe fragment contg. the reactive center of **eglin** c, were 4 .times. 10-5 M for I and >2 .times. 10-3 M for II. On the other hand, **eglin** c and its H-(8-70)-OMe fragment inhibited I and II at low concns.

AN 114:180932 CA

TI Studies on partial purification by affinity chromatography and synthetic inhibitors of leukocyte cathepsin G

AU Nagamatsu, Yoko; Tsuboi, Satoshi; Nakabayashi, Kazunori; Tsuda, Yuko; Okada, Yoshio; Yamamoto, Junichiro

CS Fac. Nutr., Kobe-Gakuin Univ., Hyogo, Japan

SO Nippon Kessen Shiketsu Gakkaishi (1990), 1(3), 203-11
CODEN: NKSGEL

DT Journal

LA Japanese

L7 ANSWER 6 OF 8 CA COPYRIGHT 2002 ACS DUPLICATE 2
AB The proteinase inhibitors **eglin** C and hirudin did not increase the survival of pigs in endotoxic shock. The **fibrinogen** consumption rate was decreased by hirudin from 36.5 to 9.8 mg/100 mL/h. **Eglin** C did not affect **fibrinogen** consumption. Hirudin, but not **eglin** C, reduced the fibrin monomer concns. in plasma. Both compds. reduced the loss of intravascular proteins. Hirudin, but not **eglin** C, reduced the pulmonary vascular resistance and the extravascular lung water. No interactions were found between the 2 proteinase inhibitors.
AN 111:108738 CA
TI Therapeutic effects of the combination of two proteinase inhibitors in endotoxin shock of the pig
AU Siebeck, M.; Hoffmann, H.; Weipert, J.; Spannagl, M.
CS Chir. Klin. Innenstadt, Ludwig-Maximilians-Univ., Munich, Fed. Rep. Ger.
SO Prog. Clin. Biol. Res. (1989), 308(Vienna Shock Forum, 2nd, 1988), 937-43
CODEN: PCBRD2; ISSN: 0361-7742
DT Journal
LA English

L7 ANSWER 7 OF 8 MEDLINE
AB Interaction of **eglin** c with three neutral proteinases (1, 2A and 2B) from horse leucocytes was investigated using synthetic and protein substrates. With N-tert-butyloxycarbonyl-L-alanine-p-nitrophenyl ester as substrate inhibition of proteinase 1 and 2A was practically complete at equimolar inhibitor concentrations (Ki below 1 nMol/l). The complex with proteinase 2B showed a dissociation constant of approximately 25 nMol/l. The latter proteinase was only partly inhibited also in the presence of azocasein, whereas almost linear inhibition was observed for all 3 proteinases with **fibrinogen** as substrate. The inhibition rate constants (kon) for horse leucocyte proteinases with **eglin** were in the range of 8 to 13 X 10(5) M-1 S-1.
AN 85225500 MEDLINE
DN 85225500 PubMed ID: 4004837
TI Inhibition of horse leucocyte proteinases by **eglin**, a proteinase inhibitor from leeches.
AU Potempa J; Dubin A; Seemuller U; Schnebli H P; Koj A
SO BIOMEDICA BIOCHIMICA ACTA, (1985) 44 (2) 335-9.
Journal code: 8304435. ISSN: 0232-766X.
CY GERMANY, EAST: German Democratic Republic
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198507
ED Entered STN: 19900320
Last Updated on STN: 19970203
Entered Medline: 19850708

L7 ANSWER 8 OF 8 CA COPYRIGHT 2002 ACS
AB The interaction of **eglin** c with 3 neutral proteinases (1, 2A, and 2B) from horse leukocytes was investigated using synthetic and protein substrates. With N-tert-butyloxycarbonyl-L-alanine p-nitrophenyl ester as substrate, the inhibition of proteinases 1 and 2A was practically complete at equimolar inhibitor concns. (Ki <1 nM). The complex with proteinase 2B

showed a dissocn. const. of .apprx.25 nM. The latter proteinase was only partly inhibited also in the presence of azocasein, whereas almost linear inhibition was obsd. for all 3 proteinases with **fibrinogen** as substrate. The inhibition rate consts. for horse leukocyte proteinases with **eglin** were in the range 8 .times. 105-13 .times. 105 M-1 s-1.

AN 102:200149 CA
TI Inhibition of horse leukocyte proteinases by **eglin**, a proteinase inhibitor from leeches
AU Potempa, J.; Dubin, A.; Seemueller, U.; Schnebli, H. P.; Koj, A.
CS Inst. Mol. Biol., Jagiellonian Univ., Krakow, Pol.
SO Biomed. Biochim. Acta (1985), 44(2), 333-7
CODEN: BBIADT
DT Journal
LA English

```
=> s plasminogen?
L8        80213 PLASMINOGEN?

=> d his

     (FILE 'HOME' ENTERED AT 16:25:16 ON 10 JUN 2002)

     FILE 'CA, BIOSIS, MEDLINE' ENTERED AT 16:25:46 ON 10 JUN 2002
L1         88756 S FIBRINOGEN?
L2          3358 S ELASTASE INHIBITOR?
L3            18 S L1 (P) L2
L4            10 DUP REM L3 (8 DUPLICATES REMOVED)
L5           886 S EGLIN?
L6            11 S L5 AND L1
L7             8 DUP REM L6 (3 DUPLICATES REMOVED)
L8         80213 S PLASMINOGEN?

=> s l8 and l1 and (l2 or l5)
L9             2 L8 AND L1 AND (L2 OR L5)

=> d 1-2 ab,bib

L9   ANSWER 1 OF 2  CA  COPYRIGHT 2002 ACS
AB   The phosphatase and tensin homol. deleted on chromosome 10 (PTEN) is a
     tumor suppressor gene with sequence homol. to tyrosine phosphatases and
     the cytoskeletal proteins tensin and auxilin.  PTEN has recently been
     shown to inhibit cell migration and the spreading and formation of focal
     adhesions.  This study investigated the role of PTEN in carcinoma
invasion
     in a lung-cancer cell line and examd. the downstream genes regulated by
     PTEN.  We have previously established a cell-line model in human lung
     adenocarcinoma with different invasive abilities and metastatic
     potentials.  Examg. PTEN gene expression in these cell lines, we found
     that a homozygous deletion in exon 5 is assocd. with high invasive
     ability.  We then constructed stable constitutive and inducible wild-type
     PTEN-overexpressed transfectants in the highly invasive cell line CL1-5.
     We found that an overexpression of PTEN can inhibit invasion in lung
     cancer cells.  To further explore the downstream genes regulated by PTEN,
     a high-d. cDNA microarray technique was used to profile gene changes
after
     PTEN overexpression.  Our results indicate a panel of genes that can be
     modulated by PTEN.  PTEN overexpression downregulated genes, including
     integrin .alpha.6, laminin .beta.3, heparin-binding epidermal growth
```

factor-like growth factor, urokinase-type **plasminogen** activator, myb protein B, Akt2, and some expressed sequence tag (EST) clones. In contrast, PTEN overexpression upregulated protein phosphatase 2A1B, ubiquitin protease (unph), secreted phosphoprotein 1, leukocyte **elastase inhibitor**, nuclear factor-.kappa.B, cAMP response element binding protein, DNA ligase 1, heat shock protein 90, and some EST genes. Northern hybridization and flow cytometry anal. also confirmed that PTEN overexpression results in the reduced expression of the integrin .alpha.6 subunit. The results of this study indicate that PTEN overexpression may inhibit lung cancer invasion by downregulation of a panel of genes including integrin .alpha.6. The cDNA microarray technique may be an effective tool to study the downstream function of a tumor suppressor gene.

AN 133:361424 CA

TI Profiling the downstream genes of tumor suppressor PTEN in lung cancer cells by complementary DNA microarray

AU Hong, Tse-Ming; Yang, Pan-Chyr; Peck, Konan; Chen, Jeremy J. W.; Yang, Shuenn-Chen; Chen, Yen-Chu; Wu, Cheng-Wen

CS Institute of Biomedical Sciences, National Health Research Institute, Graduate Institute of Molecular Biology, College of Medicine, Academia Sinica, National Taiwan University, Taipei, Taiwan

SO American Journal of Respiratory Cell and Molecular Biology (2000), 23(3), 355-363
CODEN: AJRBEL; ISSN: 1044-1549

PB American Thoracic Society

DT Journal

LA English

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 2 MEDLINE

AB Fibrin(ogen) (FGN) is important for hemostasis and wound healing and is cleared from sites of injury primarily by the **plasminogen** activator system. However, there is emerging evidence in **plasminogen** activator-deficient transgenic mice that nonplasmin pathways may be important in fibrin(ogen)olysis, as well. Given the proximity of FGN and monocytes within the occlusive thrombus at sites of vascular injury, we considered the possibility that monocytes may play an ancillary role in the degradation and clearance of fibrin. We found that monocytes possess an alternative fibrinolytic pathway that uses the integrin Mac-1, which directly binds and internalizes FGN, resulting in its lysosomal degradation. At 4 degrees C, FGN binds to U937 monocytoid cells in a specific and saturable manner with a kd of 1.8 mumol/L. Binding requires adenosine diphosphate stimulation and is calcium-dependent. At 37 degrees C, FGN and fibrin monomer (FM) are internalized and degraded at rates of 0.37 +/- 0.13 and 0.55 +/- 0.03 microgram/10(6) cells/h by U937 cells, 1.38 +/- 0.02 and 1.20 +/- 0.30 microgram/10(6) cells/h by THP-1 cells, and 2.10 +/- 0.20 and 2.52 +/- 0.18 micrograms/10(6) cells/h by human peripheral blood mononuclear cells, respectively. The serine protease inhibitors, PPACK and aprotinin, and the specific **elastase inhibitor**, AAPVCK, do not significantly inhibit degradation. However, degradation is inhibited by chloroquine, suggesting that a lysosomal pathway is involved. Factor X, a competitive ligand with FGN for the Mac-1 receptor, also blocks degradation, as does a monoclonal antibody to the alpha-subunit of Mac-1. Autoradiography of radioiodinated, internalized FGN shows that FGN proteolysis by the pathway produces a

unique degradation pattern distinct from that observed with plasmin. In a fibrin clot lysis assay, Mac-1-mediated fibrinolysis contributed significantly to total fibrinolysis. In summary, FGN is internalized and degraded by activated human monocytoid cells via Mac-1 in the absence of plasmin, thereby providing an alternative fibrinolytic pathway. Thus, in addition to the function of cell adhesion, integrins may also act as receptors that mediate the internalization and degradation of bound ligands.

AN 94003307 MEDLINE
DN 94003307 PubMed ID: 8400291
TI Fibrin(ogen) is internalized and degraded by activated human monocytoid cells via Mac-1 (CD11b/CD18): a nonplasmin fibrinolytic pathway.
AU Simon D I; Ezratty A M; Francis S A; Rennke H; Loscalzo J
CS Brockton/West Roxbury V.A. Medical Center, MA.
NC HL40411 (NHLBI)
HL43344 (NHLBI)
HL48743 (NHLBI)
+
SO BLOOD, (1993 Oct 15) 82 (8) 2414-22.
Journal code: 7603509. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199311
ED Entered STN: 19940117
Last Updated on STN: 19940117
Entered Medline: 19931123

=> d his

(FILE 'HOME' ENTERED AT 16:25:16 ON 10 JUN 2002)

FILE 'CA, BIOSIS, MEDLINE' ENTERED AT 16:25:46 ON 10 JUN 2002
L1 88756 S FIBRINOGEN?
L2 3358 S ELASTASE INHIBITOR?
L3 18 S L1 (P) L2
L4 10 DUP REM L3 (8 DUPLICATES REMOVED)
L5 886 S EGLIN?
L6 11 S L5 AND L1
L7 8 DUP REM L6 (3 DUPLICATES REMOVED)
L8 80213 S PLASMINOGEN?
L9 2 S L8 AND L1 AND (L2 OR L5)

=> s l2 or l5
L10 4120 L2 OR L5

=> s l10 same l1 and l8
MISSING OPERATOR L10 SAME
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l10 same l1 same l8
MISSING OPERATOR L10 SAME
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l10 and l1 and l8
L11 2 L10 AND L1 AND L8

```
=> d 1-2

L11  ANSWER 1 OF 2  CA  COPYRIGHT 2002 ACS
AN   133:361424  CA
TI   Profiling the downstream genes of tumor suppressor PTEN in lung cancer
     cells by complementary DNA microarray
AU   Hong, Tse-Ming; Yang, Pan-Chyr; Peck, Konan; Chen, Jeremy J. W.; Yang,
     Shuenn-Chen; Chen, Yen-Chu; Wu, Cheng-Wen
CS   Institute of Biomedical Sciences, National Health Research Institute,
     Graduate Institute of Molecular Biology, College of Medicine, Academia
     Sinica, National Taiwan University, Taipei, Taiwan
SO   American Journal of Respiratory Cell and Molecular Biology (2000), 23(3),
     355-363
     CODEN: AJRBEL; ISSN: 1044-1549
PB   American Thoracic Society
DT   Journal
LA   English
RE.CNT  35    THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11  ANSWER 2 OF 2     MEDLINE
AN   94003307     MEDLINE
DN   94003307   PubMed ID: 8400291
TI   Fibrin(ogen) is internalized and degraded by activated human monocytoid
     cells via Mac-1 (CD11b/CD18): a nonplasmin fibrinolytic pathway.
AU   Simon D I; Ezratty A M; Francis S A; Rennke H; Loscalzo J
CS   Brockton/West Roxbury V.A. Medical Center, MA.
NC   HL40411 (NHLBI)
     HL43344 (NHLBI)
     HL48743 (NHLBI)
     +
SO   BLOOD, (1993 Oct 15) 82 (8) 2414-22.
     Journal code: 7603509. ISSN: 0006-4971.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Abridged Index Medicus Journals; Priority Journals
EM   199311
ED   Entered STN: 19940117
     Last Updated on STN: 19940117
     Entered Medline: 19931123


=> d his

     (FILE 'HOME' ENTERED AT 16:25:16 ON 10 JUN 2002)

     FILE 'CA, BIOSIS, MEDLINE' ENTERED AT 16:25:46 ON 10 JUN 2002
L1         88756 S FIBRINOGEN?
L2          3358 S ELASTASE INHIBITOR?
L3            18 S L1 (P) L2
L4            10 DUP REM L3 (8 DUPLICATES REMOVED)
L5           886 S EGLIN?
L6            11 S L5 AND L1
L7             8 DUP REM L6 (3 DUPLICATES REMOVED)
L8         80213 S PLASMINOGEN?
L9             2 S L8 AND L1 AND (L2 OR L5)
L10         4120 S L2 OR L5
L11            2 S L10 AND L1 AND L8
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=> s l10 (p) l1 (p) l8
L12           0 L10 (P) L1 (P) L8

=> s l10 (p) l1
L13          26 L10 (P) L1

=> dup rem
ENTER L# LIST OR (END):l13
PROCESSING COMPLETED FOR L13
L14           15 DUP REM L13 (11 DUPLICATES REMOVED)

=> d 1-15 ab,bib

L14  ANSWER 1 OF 15  CA  COPYRIGHT 2002 ACS
AB   The invention provides a method for reducing or preventing adhesions
which
     would form in a patient during or after surgery, said method comprising
     administering to said patient an effective amt. of a fibrinogen prepn.
     contg. a non-plasmin acting fibrinolysis inhibitor.  The invention also
     provides the use of a non-plasmin acting fibrinolysis inhibitor in the
     prepn. of a fibrinogen prepn. for the redn. or prevention of postsurgical
     adhesions.
AN   136:289068  CA
TI   Fibrinogen plus a non-plasmin-acting fibrinolysis inhibitor for the
     reduction or prevention of adhesion formation following surgery
IN   Redl, Heinz
PA   Baxter International Inc., USA; Baxter Healthcare S.A.
SO   PCT Int. Appl., 16 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE            APPLICATION NO.  DATE
     ---------------   ----  --------        ---------------  --------
PI   WO 2002030445      A2   20020418        WO 2001-US32043  20011012
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
             US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI US 2000-240438P   P    20001013

L14  ANSWER 2 OF 15  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN   2001:131559  BIOSIS
DN   PREV200100131559
TI   The effect of virus inactivation on coagulation factors in therapeutic
     plasma.
AU   Zeiler, T. (1); Wittmann, G.; Zimmermann, R.; Hintz, G.; Huhn, D.; Riess,
     H.
CS   (1) Department of Transfusion Medicine and Haemostaseology, University
     Clinics, Philipps-University Marburg, Berlin:
zeiler@mailer.uni-marburg.de
     Germany
SO   British Journal of Haematology, (December, 2000) Vol. 111, No. 3, pp.
     986-987. print.
```

ISSN: 0007-1048.
DT Letter
LA English
SL English

L14 ANSWER 3 OF 15 CA COPYRIGHT 2002 ACS
AB A **fibrinogen**-based tissue adhesive (fibrin glue) contains an **elastase inhibitor** to stabilize the adhesive in vivo against premature fibrinolysis. The **elastase inhibitor** (e.g. **eglin**, elastase-.alpha.1-proteinase inhibitor, .alpha.1-antiprotease, elafin, leukocyte proteinase inhibitor) is effective even in the absence of plasmin inhibitors such as aprotinin, and is preferably a human or recombinant human protein. It is used in a proportion of .gtoreq.10-6 U/g **fibrinogen**, preferably 10-3-10 U/g.
AN 130:213685 CA
TI Fibrinogen-based tissue adhesive
IN Redl, Heinz; Schlag, Guenther; Eibl, Johann
PA Immuno Aktiengesellschaft, Austria
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9911301	A1	19990311	WO 1998-AT202	19980826
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AT 9701449	A	19990715	AT 1997-1449	19970828
	AT 406120	B	20000225		
	AU 9889637	A1	19990322	AU 1998-89637	19980826
	EP 1007109	A1	20000614	EP 1998-941134	19980826
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
	JP 2001514050	T2	20010911	JP 2000-508402	19980826
PRAI	AT 1997-1449	A	19970828		
	WO 1998-AT202	W	19980826		

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 15 CA COPYRIGHT 2002 ACS DUPLICATE 1
AB Upon stimulation, polymorphonuclear leukocytes (PMNs) release potent serine proteases, i.e. elastase, cathepsin G and proteinase 3, which contribute to the degrdn. of tissue and plasma components. Here, we describe the development of a plasma test to assess PMN-mediated **fibrinogenolysis** as a biochem. marker for actual PMN-derived proteolysis in vivo, useful for monitoring therapeutic efficacy, i.e. of **elastase inhibitors**. We generated a monoclonal antibody (MAb), designated 1-1/B3, with a high affinity for elastase-degraded **fibrinogen** (EDF). The epitope for 1-1/B3 becomes exposed in a time-dependent manner during digestion of **fibrinogen** with purified PMN-derived serine proteases and with isolated PMNs in vitro.

However, 1-1/B3 does not react with plasma **fibrinogen** or with fibrin(ogen) degrdn. products generated by plasmin or by other active proteases that may occur locally, i.e. metalloproteases and lysosomal cathepsins. On the basis of MAb 1-1/B3, we developed a plasma test for the assessment of PMN-mediated fibrin(ogen) degrdn. products (PMN-FDP). In a panel of control plasmas, we obsd. concns. of PMN-FDP of 8.cntdot.2 .+-. 0.cntdot.9 ng mL-1 (n = 18). These values were increased twofold in patients with .alpha.1-proteinase inhibitor deficiency (18.cntdot.6 .+-. 3.cntdot.3 ng mL-1; n = 12; P < 0.cntdot.0001) and even more in patients with sepsis (365.cntdot.7 .+-. 97.cntdot.7 ng mL-1; n = 16; P < 0.cntdot.0001). Furthermore, synovial tissue exts. from patients with rheumatoid arthritis contained increased levels of PMN-FDP, compared with synovial tissue exts. (P < 0.cntdot.005) from patients with osteoarthritis.

AN 126:235523 CA

TI An enzyme immunoassay for polymorphonuclear leukocyte-mediated fibrinogenolysis

AU Bos, R.; Van Leuven, C. J. M.; Stolk, J.; Hiemstra, P. S.; Ronday, H. K.; Nieuwenhuizen, W.

CS TNO-Prevention and Health, Division of Vascular and Connective Tissue Research, Leiden, 2301 CE, Neth.

SO Eur. J. Clin. Invest. (1997), 27(2), 148-156
CODEN: EJCIB8; ISSN: 0014-2972

PB Blackwell

DT Journal

LA English

L14 ANSWER 5 OF 15 CA COPYRIGHT 2002 ACS DUPLICATE 2

AB The relation of biol. markers of extracellular matrix (plasma elastin peptides and **elastase inhibitors**) to the clin. history of cardiovascular diseases and risk factors for atherosclerosis were examd. in a large population study (the EVA Study) on vascular and cognitive aging performed in 1389 men and women 59-71 yr. A moderate decrease in elastin peptides was obsd. in women with a self-reported history of coronary heart disease and stroke as well as with diabetes. Similar but non-significant trends were found in men. Furthermore, elastin peptides were significantly and pos. correlated to HDL-cholesterol and apolipoprotein A1 in both sexes. **Elastase inhibitor** titers were significantly higher in women than in men. A moderate increase was found in men and women with a history of coronary heart disease that reached significance level after pooling both sexes. Furthermore, **elastase inhibitor** titers were significantly and pos. related to **fibrinogen** and C reactive protein in either sex. No consistent assocns. were obsd. between both biol. markers of extracellular matrix and age, blood pressure, body mass index and tobacco or alc. consumption. These results suggested that a decrease in elastin peptides and an increase in **elastase inhibitors** might be assocd. with risk factors of atherogenesis as well as with atherosclerosis-related diseases.

AN 127:93576 CA

TI Aging of the vascular wall: serum concentration of elastin peptides and elastase inhibitors in relation to cardiovascular risk factors. The EVA study

AU Bizbiz, L.; Alperovitch, A.; Robert, L.

CS EVA Group, Lab. Biol. Cellulaire, Univ. Paris VII, Paris, 75005, Fr.

SO Atherosclerosis (Shannon, Ireland) (1997), 131(1), 73-78
CODEN: ATHSBL; ISSN: 0021-9150

PB Elsevier

DT Journal

LA English

L14 ANSWER 6 OF 15 CA COPYRIGHT 2002 ACS DUPLICATE 3
AB Leukocyte initiation of coagulation preserves the hematostatic balance and may aberrantly contribute to vascular injury. In addn. to the extrinsic activation mediated by tissue factor: factor VIIa, monocytes express an alternative procoagulant response after binding of the zymogen factor X to the integrin Mac-1 (CD11b/CD18). Here, factor X-activating activity was found in purified monocyte granules, and coincided with size-chromatographed fractions contg. cathepsin G. In contrast, elastase-contg. granule fractions did not activate factor X. In the presence of Ca2+ ions, purified cathepsin G, but not elastase, cleaved factor X to a .apprx.54 kDa catalytically active deriv., structurally indistinguishable from the procoagulant product generated on monocytes after binding to Mac-1. Factor X activation by purified cathepsin G involved limited proteolysis of a novel Leu177-Leu178 peptide bond in the zymogen's activation peptide. Cathepsin G activation of factor X was completely inhibited by .alpha.1 antitrypsin, .alpha.1 antichymotrypsin, or soybean trypsin inhibitor, or by a neutralizing antiserum to cathepsin G, while **eglin**, or an anti-elastase antibody, were ineffective. Affinity chromatog. on active-site-dependent inhibitors Glu-Gly-Arg-chloromethyl ketone or benzamidine completely abolished factor Xa activity generated by cathepsin G. Cathepsin G was not constitutively detected on the monocyte surface by flow cytometry. However, inflammatory stimuli, including formyl peptide or phorbol ester, or Mac-1 engagement with its ligands **fibrinogen**, factor X or serum-opsonized zymosan, triggered monocyte degranulation and cathepsin G activation of factor X. These findings demonstrate that monocytes can alternatively initiate coagulation in a sequential three-step cascade, including (i) binding of factor X to Mac-1, (ii) discharge of azurophil granules, and (iii) limited proteolytic activation of membrane-bound factor X by cathepsin G. By rapidly forming thrombin and factor Xa in a protected membrane microenvironment, this pathway may contribute a priming signal for clotting, anticoagulation and visual cell signal transduction, in vivo.
AN 126:17537 CA
TI Activation of Mac-1 (CD11b/CD18)-bound factor X by released cathepsin G defines an alternative pathway of leukocyte initiation of coagulation
AU Plescia, Janet; Altieri, Dario C.
CS Boyer Center Molecular Medicine, Yale University School Medicine, New Haven, CT, 06536, USA
SO Biochem. J. (1996), 319(3), 873-879
CODEN: BIJOAK; ISSN: 0264-6021
PB Portland Press
DT Journal
LA English

L14 ANSWER 7 OF 15 MEDLINE
AB The patterns of degradation and the influence of factor XIII polymerization on fibrin stability were examined in vitro following incubation with leukocyte elastase. In vivo experiments, various factor XIII-polymerized fibrin clots were implanted subcutaneously in mice to evaluate the stability of clots in the extravascular space. Both in vitro and in vivo lysis proceeded faster with nonpolymerized fibrin and was not influenced by the presence of cross-linked alpha 2-plasmin inhibitor. In vivo lysis of implanted clots was prevented by elastatinal, powerful

elastase inhibitor, suggesting that granulocyte elastase is chiefly responsible for clot lysis in the extravascular space. To further extend investigations on the mechanisms of fibrinolysis in tissues, we evaluated fibrin and its degradation products in the synovial space. Expression of factor XIII in synovial cells and activities of coagulation factors, fibrinolytic enzymes, and inhibitors were investigated in the synovial fluid of rheumatoid arthritis patients. Immunohistochemical analysis showed deposits of insoluble fibrin on synovial membranes and pannus to an extent related to the progression of the disease. Factor XIII was expressed by fibroblasts and macrophages in the early stages of the disease, whereas in advanced stages factor XIII staining was associated with fibrin. The reduction of certain coagulation factors and high level of thrombin-antithrombin complexes in synovial fluid show a steady activation of the coagulation cascade. The evaluation of **fibrinogen** degradation products and the pattern of degradation of synovial fibrin(ogen) suggest the participation of leukocyte elastase in fibrin(ogen) lysis in synovial tissue of rheumatoid arthritis.

AN 97192399 MEDLINE
DN 97192399 PubMed ID: 9122713
TI Fibrin degradation in the synovial fluid of rheumatoid arthritis patients:
a model for extravascular fibrinolysis.
AU Carmassi F; de Negri F; Morale M; Song K Y; Chung S I
CS 2nd Medical Clinic, University of Pisa, Italy.
SO SEMINARS IN THROMBOSIS AND HEMOSTASIS, (1996) 22 (6) 489-96. Ref: 90
Journal code: 0431155. ISSN: 0094-6176.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199704
ED Entered STN: 19970506
Last Updated on STN: 19970506
Entered Medline: 19970424

L14 ANSWER 8 OF 15 CA COPYRIGHT 2002 ACS
AB Incubation of human blood with the secretagogue A23187 resulted in the formation of increased plasma concns. of polymorphonuclear leukocyte (PMN) elastase:.alpha.1 proteinase inhibitor (PMNE:.alpha.1PI) complex as well as A.alpha.(1-21) fibrinopeptide [A.alpha.(1-21)]. The formation of these species was both time and A23187 concn. dependent. Using a sandwich ELISA and a RIA, we detd. the comparative potencies of several compds. to inhibit the formation of PMNE:.alpha.1PI complexes and A.alpha.(1-21), resp. L-658,758, a substituted cephalosporin, essentially irreversible elastase inhibitor, inhibited the formation of PMNE:.alpha.1PI and A.alpha.(1-21) with IC50 values of 38 and 15 .mu.M, resp. L-683,845, a monocyclic .beta.-lactam, was much more potent against isolated PMNE than L-658,758. However in this system it was approx. equiv. to L-658,758 with an IC50 of 15 .mu.M against both species. ICI-200,880, a competitive slow-binding elastase inhibitor, was significantly less potent to inhibit A.alpha.(1-21), having an IC50 of 75 .mu.M, while Declaben, a reversible noncompetitive inhibitor, was inactive at concns. as great as 200 .mu.M. We propose that evaluating inhibitors in the complex milieu of blood will

provide a useful method to predict their therapeutic potential in vivo.
AN 123:187603 CA
TI Formation of polymorphonuclear leukocyte elastase:.alpha.1 proteinase inhibitor complex and A.alpha.(1-21) fibrinopeptide in human blood stimulated with the calcium ionophore A23187. A model to characterize inhibitors of polymorphonuclear leukocyte elastase
AU Pacholok, Stephen G.; Davies, Philip; Dorn, Conrad; Finke, Paul; Hanlon, William A.; Mumford, Richard A.; Humes, John L.
CS Merck Res. Labs., Rahway, NJ, 07065, USA
SO Biochem. Pharmacol. (1995), 49(10), 1513-20
CODEN: BCPCA6; ISSN: 0006-2952
DT Journal
LA English

L14 ANSWER 9 OF 15 CA COPYRIGHT 2002 ACS DUPLICATE 4
AB Acute respiratory failure is a common complication in patients with disseminated intravascular coagulation assocd. with sepsis. To elucidate the role of coagulation abnormalities in acute lung injury in sepsis, the authors investigated the effect of anticoagulants on the pulmonary vascular injury in rat induced by lipopolysaccharide (LPS). When administered i.v., LPS (5 mg/kg body wt.) increased the accumulation of 111indium-labeled neutrophils in lung 30 min after administration. Subsequently, the pulmonary vascular permeability and the serum level of fibrin and **fibrinogen** degrdn. products (E) [FDP (E)] increased and remained elevated for several hours. Neither heparin alone, heparin plus antithrombin III, or dansyl-Glu-Gly-Arg-chloromethyl ketone-treated factor Xa, a selective inhibitor of thrombin generation, prevented LPS-induced vascular injury 6 h after LPS administration, whereas these substances inhibited the increase in serum FDP (E) at that time. LPS-induced pulmonary vascular injury was attenuated in rats with methotrexate-induced leukocytopenia or treated with ONO-5046, a potent granulocyte **elastase inhibitor**, although ONO-5046 did not inhibit the LPS-induced increase in serum FDP (E). Thus, activated leukocytes play a more important role than coagulation abnormalities in the pathogenesis of LPS-induced pulmonary vascular injury in an exptl. rat model of endotoxemia.
AN 122:262617 CA
TI Endotoxin-induced pulmonary vascular injury is mainly mediated by activated neutrophils in rats
AU Uchiba, Mitsuhiro; Okajima, Kenji; Murakami, Kazunori; Okabe, Hiroaki; Takatsuki, Kiyoshi
CS Department of Medicine, Kumamoto University Medical School, Kumamoto, Japan
SO Thromb. Res. (1995), 78(2), 117-25
CODEN: THBRAA; ISSN: 0049-3848
DT Journal
LA English

L14 ANSWER 10 OF 15 CA COPYRIGHT 2002 ACS
AB A simple purifn. method which is able to sep. leukocyte cathepsin G (I) from leukocyte elastase (II) is described. I was purified on an affinity column contg. Suc-Tyr-D-Leu-D-Val-pNA-Sepharose (Suc = succinyl; pNA = p-nitroanilide). I in leukocyte exts. adsorbed to the column at low concns. of NaCl (0.2M), and was eluted with Tris-HCl buffer (0.1M, pH 7.5) contg. 2M NaCl. The purified I prepn. contained no II activity. Although the proteolytic activity of I against **fibrinogen** and fibrin was very weak compared with that of II, I acted synergistically with II in the

fibrinogenolysis. Furthermore, the effect was dependent on the amt. of I. The inhibitory effects of **eglin** c fragments for I and II were different. The Ki values of the H-(41-49)-OMe fragment contg. the reactive center of **eglin** c, were 4 .times. 10-5 M for I and >2 .times. 10-3 M for II. On the other hand, **eglin** c and its H-(8-70)-OMe fragment inhibited I and II at low concns.

AN 114:180932 CA
TI Studies on partial purification by affinity chromatography and synthetic inhibitors of leukocyte cathepsin G
AU Nagamatsu, Yoko; Tsuboi, Satoshi; Nakabayashi, Kazunori; Tsuda, Yuko; Okada, Yoshio; Yamamoto, Junichiro
CS Fac. Nutr., Kobe-Gakuin Univ., Hyogo, Japan
SO Nippon Kessen Shiketsu Gakkaishi (1990), 1(3), 203-11
CODEN: NKSGEL
DT Journal
LA Japanese

L14 ANSWER 11 OF 15 CA COPYRIGHT 2002 ACS DUPLICATE 5
AB Tryptase from human mast cells has been shown (in vitro) to catalyze the destruction of **fibrinogen** and high-mol.-wt. kininogen as well as the activation of complement C3a and collagenase. Although large amts. of tryptase are released in tissues by degranulating mast cells and levels .ltoreq.1000 ng/mL have been measured in the circulation following systemic anaphylaxis, no specific physiol. inhibitor has yet been found for the protease. The current work tests several more inhibitors for their effects on tryptase and examines any effect of tryptase on these inhibitors. First, antileukoprotease and low-mol.-wt. **elastase inhibitor** from human lung and hirudin and antithrombin III had no effect on tryptase activity in vitro. Second, the possibility that tryptase, being insensitive to the effects of inhibitors, might instead destroy them was also considered. Tryptase failed to cleave and inactivate antileukoprotease, low-mol.-wt. **elastase inhibitor**, .alpha.1-protease inhibitor, .alpha.2-macroglobulin, and antithrombin III. Third, based on the knowledge that tryptase stability is regulated by its interaction with heparin, antithrombin III was used as a model heparin-binding protein to demonstrate that a protein competitor for heparin-binding sites, presumably by displacement of tryptase, destabilizes this enzyme. Conversely, tryptase, in excess, blocked the binding of antithrombin III to heparin, thereby attenuating the heparin-mediated inhibition of thrombin by antithrombin III.

AN 112:114729 CA
TI Interactions of human mast cell tryptase with biological protease inhibitors
AU Alter, Stephen C.; Kramps, Johannes A.; Janoff, Aaron; Schwartz, Lawrence B.
CS Dep. Med., Med. Coll. Virginia, Richmond, VA, 23298, USA
SO Arch. Biochem. Biophys. (1990), 276(1), 26-31
CODEN: ABBIA4; ISSN: 0003-9861
DT Journal
LA English

L14 ANSWER 12 OF 15 CA COPYRIGHT 2002 ACS DUPLICATE 6
AB The proteinase inhibitors **eglin** C and hirudin did not increase the survival of pigs in endotoxic shock. The **fibrinogen** consumption rate was decreased by hirudin from 36.5 to 9.8 mg/100 mL/h. **Eglin** C did not affect **fibrinogen** consumption. Hirudin, but not **eglin** C, reduced the fibrin monomer concns. in plasma. Both compds. reduced the loss of intravascular proteins. Hirudin, but not

eglin C, reduced the pulmonary vascular resistance and the extravascular lung water. No interactions were found between the 2 proteinase inhibitors.

AN 111:108738 CA
TI Therapeutic effects of the combination of two proteinase inhibitors in endotoxin shock of the pig
AU Siebeck, M.; Hoffmann, H.; Weipert, J.; Spannagl, M.
CS Chir. Klin. Innenstadt, Ludwig-Maximilians-Univ., Munich, Fed. Rep. Ger.
SO Prog. Clin. Biol. Res. (1989), 308(Vienna Shock Forum, 2nd, 1988), 937-43
CODEN: PCBRD2; ISSN: 0361-7742
DT Journal
LA English

L14 ANSWER 13 OF 15 MEDLINE
AB Interaction of **eglin** c with three neutral proteinases (1, 2A and 2B) from horse leucocytes was investigated using synthetic and protein substrates. With N-tert-butyloxycarbonyl-L-alanine-p-nitrophenyl ester as substrate inhibition of proteinase 1 and 2A was practically complete at equimolar inhibitor concentrations (Ki below 1 nMol/l). The complex with proteinase 2B showed a dissociation constant of approximately 25 nMol/l. The latter proteinase was only partly inhibited also in the presence of azocasein, whereas almost linear inhibition was observed for all 3 proteinases with **fibrinogen** as substrate. The inhibition rate constants (kon) for horse leucocyte proteinases with **eglin** were in the range of 8 to 13 X 10(5) M-1 S-1.
AN 85225500 MEDLINE
DN 85225500 PubMed ID: 4004837
TI Inhibition of horse leucocyte proteinases by eglin, a proteinase inhibitor from leeches.
AU Potempa J; Dubin A; Seemuller U; Schnebli H P; Koj A
SO BIOMEDICA BIOCHIMICA ACTA, (1985) 44 (2) 335-9.
Journal code: 8304435. ISSN: 0232-766X.
CY GERMANY, EAST: German Democratic Republic
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198507
ED Entered STN: 19900320
Last Updated on STN: 19970203
Entered Medline: 19850708

L14 ANSWER 14 OF 15 CA COPYRIGHT 2002 ACS
AB The interaction of **eglin** c with 3 neutral proteinases (1, 2A, and 2B) from horse leukocytes was investigated using synthetic and protein substrates. With N-tert-butyloxycarbonyl-L-alanine p-nitrophenyl ester as substrate, the inhibition of proteinases 1 and 2A was practically complete at equimolar inhibitor concns. (Ki <1 nM). The complex with proteinase 2B showed a dissocn. const. of .apprx.25 nM. The latter proteinase was only partly inhibited also in the presence of azocasein, whereas almost linear inhibition was obsd. for all 3 proteinases with **fibrinogen** as substrate. The inhibition rate consts. for horse leukocyte proteinases with **eglin** were in the range 8 .times. 105-13 .times. 105 M-1 s-1.
AN 102:200149 CA
TI Inhibition of horse leukocyte proteinases by eglin, a proteinase inhibitor

from leeches
AU Potempa, J.; Dubin, A.; Seemueller, U.; Schnebli, H. P.; Koj, A.
CS Inst. Mol. Biol., Jagiellonian Univ., Krakow, Pol.
SO Biomed. Biochim. Acta (1985), 44(2), 333-7
CODEN: BBIADT
DT Journal
LA English

L14 ANSWER 15 OF 15 CA COPYRIGHT 2002 ACS
AB Inhibitors for chymotrypsin, trypsin, elastase, and plasmin were studied in 18 horses with **fibrinogen** plate electrophoresis. Plasmin was mainly inhibited by .alpha.2-macroglobulin (.alpha.2M). Besides .alpha.2M, an anodically migrating group of inhibitors in the albumin-prealbumin region was responsible for inhibition of chymotrypsin, trypsin, and elastase. These inhibitors were heterogeneous. Three inhibitors for chymotrypsin, 3 for trypsin, and .gtoreq.2 for elastase were identified. Not more than 2 inhibitors for 1 enzyme were present in the serum of a single animal. The banding patterns showed individual differences. Four patterns for chymotrypsin and 3 for trypsin could be distinguished in the 18 horses studied. **Elastase inhibitors** showed fewer individual differences. This may partly be due to the low resolving power of the method used. The possible implications of the heterogeneity of the inhibitors for the pathogenesis of chronic obstructive lung diseases are discussed.
AN 90:135633 CA
TI Electrophoretic analysis of protease inhibitors in horses serum
AU Von Fellenberg, R.
CS Inst. Veterinaerphysiol., Univ. Zurich, Zurich, Switz.
SO Schweiz. Arch. Tierheilkd. (1978), 120(12), 631-42
CODEN: SATHAA; ISSN: 0036-7281
DT Journal
LA German

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(FILE 'HOME' ENTERED AT 16:25:16 ON 10 JUN 2002)

FILE 'CA, BIOSIS, MEDLINE' ENTERED AT 16:25:46 ON 10 JUN 2002
L1 88756 S FIBRINOGEN?
L2 3358 S ELASTASE INHIBITOR?
L3 18 S L1 (P) L2
L4 10 DUP REM L3 (8 DUPLICATES REMOVED)
L5 886 S EGLIN?
L6 11 S L5 AND L1
L7 8 DUP REM L6 (3 DUPLICATES REMOVED)
L8 80213 S PLASMINOGEN?
L9 2 S L8 AND L1 AND (L2 OR L5)
L10 4120 S L2 OR L5
L11 2 S L10 AND L1 AND L8
L12 0 S L10 (P) L1 (P) L8
L13 26 S L10 (P) L1
L14 15 DUP REM L13 (11 DUPLICATES REMOVED)

=> s l1 (p) l8
L15 8641 L1 (P) L8